

IN THE DRAWINGS

Replacement sheets of FIGS. 1 and 3 are attached to this Amendment.

REMARKS

In paragraph 1 of the Office Action the Examiner objected to Figures 1 and 3 under 37 CFR 1.84(p)(5). Replacement Sheets are attached hereto that specifically point out the third feed receptacle element 4. Paragraph 0037 clearly indicates that the third feed receptacle element 4 is the one with a “small quantity of glycerol 37” and is located between first feed receptacle 2 and second feed receptacle 3. No new matter has been added.

It is requested that the Replacement Sheets be admitted and the objection be withdrawn.

In paragraph 2 of the Office Action the Examiner objected to the specification because of the spelling mistake with regard to “*Pichia pastoris*” on page 4, line 13 of the specification. The specification has been amended herewith and it is therefore requested that the objection be withdrawn.

In paragraph 3 of the Office Action the Examiner objected to claim 11 because of a spelling mistake with regard to “*Pichia pastoris*”. The claim term has been amended to fix the spelling and it is therefore requested that the objection be withdrawn.

In paragraphs 4-8 the Examiner rejected claims 6 and 17 under 35 U.S.C. 112, second paragraph.

Reconsideration is requested.

The term “induction” in claim 6 refers to the beginning of the production of recombinant proteins. Support for this claim term is found in the specification as filed and specifically at paragraph 0035 of published application.

The term “essentially” has been removed from claim 17. Applicants submit that the claim language is no longer indefinite.

Based on the above remarks and amendments it is requested that the above 112 rejections be withdrawn.

In paragraphs 9-15 the Examiner rejected claims 1,2, 4, 8-10, 15-18 and 20 under 35 USC 102(b) as being anticipated by U.S. 6,214,574 (hereinafter “Kopf”).

Reconsideration is requested.

Claim 1 have been amended to more clearly point out that the present invention employs a single downstream cross-flow filtration unit (5), and that the feed receptacle (2, 3, 4) is connected to the bioreactor (1) by a feed line (7, 9, 11). Further, claim 1 has been amended to point out that the bioreactor is connected to the cross flow filtration unit (5) by the conveying line (13) and the retentate line (17) and that filtration unit (5) is connected to a harvest receptacle (16) by permeate line (15). Also, claim 1 has been amended to point out that the feed receptacles are upstream of the bioreactor, and the harvest receptacles (16, 18) and cross flow filtration unit (5) are located downstream of the bioreactor (1). Further, claims 1 and 17 have been amended to more particularly point out that a second harvest receptacle (18) for storing retentate is connected to the bioreactor (1) via harvest line (19). Support for these amendments can be found in Fig. 1 and in paragraphs 0030-0043 of the present application. No new matter has been added.

The device and method taught by the Kopf reference differs substantially from the device and method of the present invention. Specifically, the feed receptacles (163, 148, 166) of Kopf are located both upstream and downstream of the tangential flow growth device (144) (which the Examiner has deemed an equivalent to the bioreactor (1) of the present invention) and the tangential filtration unit (164). Also, the auxiliary tanks (158, 174) (which the Examiner has deemed an equivalent to the harvest receptacles (16, 18) of the present invention) are located both upstream and downstream of the tangential flow growth device (144) and the tangential filtration unit (164). Because of the locations of the feed receptacles and harvest containers of the Kopf reference, it is necessary that the medium must flow over a possibly contaminated line (161), which connects the filtration unit (164) to the growth device (144) from both upstream and downstream directions. While Kopf possesses stopcocks (183) and a four way valve (182), the medium and retentate is still flowing over the same tubing. In light of these major differences, Applicants submit that the method and device of Kopf differ from the method and device of the present invention.

In order to construct a simple and efficient cross-flow filtration device with reduced contamination potential, the Applicants have developed a system that contains feed receptacles (2,3,4) downstream of the cross-flow filtration device (5) and bioreactor (1) and harvest receptacles (16, 18) upstream of the cross-flow filtration device (5) and bioreactor (1). In contrast the system as taught by Kopf has the potential to lead to cross

contamination of the medium and retentate. The contamination can occur because the medium must flow through the same tubing (161) before and after it has been acted upon by the tangential flow growth device (144) and the filtration unit (164). This is especially true for medium that must flow from the filtration unit (164) and back to the growth device (144) through the four way valve (182). In sharp contrast, the present invention has dedicated tubing for flow from the feed receptacles (2, 3, 4) to the bioreactor (1) along feed lines (7, 9, 11), and then from the bioreactor (1) to the cross flow filter (5) along conveying line 13, and then further separate and dedicated tubing from the cross flow filter (5) to either of the harvest containers (16, 18), via permeate line 15 or harvest line 19, or back to the bioreactor (1) via the retentate line (17). This avoids the problems of cross contamination inherent in the Kopf system.

Further, Kopf does not disclose the specific method or device by which the retentate is re-circulated back to the bioreactor (1) and can then be removed from the bioreactor by harvest line (19) for storage in a second harvest container (18). (See Fig. 1 and paragraphs 0031 and 0038 of the present application).

Based on the differences between the pathways for medium, permeate and retentate flowing between the feed receptacles, bioreactor, cross-flow filtration unit and harvest receptacles of Kopf and the requirements in the present claims for feed lines, permeate lines, retentate lines and conveying lines, and upstream and downstream locations for feed receptacles and harvest receptacles, Applicants submit that each and every element of claims 1 and 17, and all dependent claims thereon, are not disclosed by Kopf. It is therefore requested that the 102(b) rejection be withdrawn.

In paragraphs 16-26 of the Office Action the Examiner rejected claims 3, 5-7, 11-14, 19 and 21 under 35 USC 103(a) as being unpatentable over Kopf in view of CAB8-Computer Applications in Biotechnology, June 25-27, 2001 (hereinafter "Cornelissen et al.").

Reconsideration is requested.

As discussed above in detail, Kopf does not teach or suggest each and every element of claims 1 or 17 of the present application. Applicant submits that because Kopf does not teach or suggest a method or device that uses upstream feed receptacles, a cross flow filter downstream of a bioreactor, harvest receptacles located downstream of the bioreactor and cross-flow filter, and wherein all medium, retentate and permeate

flows along dedicated tubing, Kopf does render claims 1 or 17 of the present application obvious.

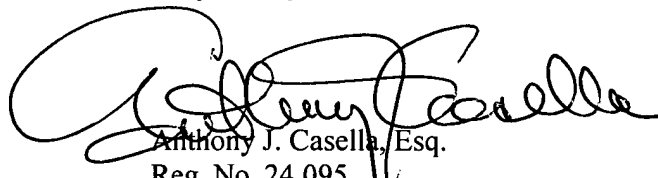
Cornelissen et al discloses a method for production of recombinant proteins. However, Cornelissen does not alleviate all of the deficiencies of Kopf. Specifically, Cornelissen does not teach a method or device that employs a second harvest receptacle (18) for a cell-contaminated harvest of the retentate that is connected to the bioreactor (1) by way of a harvest line (19).

Because, Cornelissen et al. does not teach or suggest the use of a second harvest receptacle for storing retentate, wherein said second harvest unit is connected to a cross-flow filtration unit by dedicated lines as required by the claims of the present application it is requested that the 103(a) rejection be withdrawn.

Based upon the above amendments and remarks, Applicants respectfully submit that amended claims 1-21 are allowable over the prior art and that the present application is in proper form for allowance.

Favorable consideration and early allowance is respectfully requested and earnestly solicited.

Respectfully submitted,



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